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Cardiac Transplantation in Patients Over 50 Years of Age

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Sixty-two patients underwent cardiac transplantation at the University of Arizona from March 1979 to March 1985. Thirteen patients (11 men and 2 women) were over 50 years of age at the time of transplantation and 49 were under the age of 50. The mean age (± SEM) of the patients over 50 was 53 ± 1 years. Eight of these patients were treated with conventional immunosuppressive therapy (azathioprine, prednisone and rabbit antithymocyte globulin) and five, beginning in January 1983, were treated with cyclosporine, prednisone and rabbit antithymocyte globulin.

Early mortality (0 to 90 days) was 16% in the group over 50 versus 18% for those under 50. The late mortality (> 90 days) was 36 and 33%, respectively. In both groups, rejection and infection were the principal causes of death. The incidence of infection was 1.9 ± 0.5 episodes per patient in those patients over 50 and 1.9 ± 0.4 in those under 50. The incidence of rejection was 1.3 episodes per patient-year in patients over 50 and 1.7 episodes per patient-year in those under 50. Actuarial survival at 1 year was 72 ± 14% in the group over 50 and 66 ± 7% in the group under 50 years of age.

These data indicate that the results of cardiac transplantation for patients over 50 do not differ significantly from those for patients under 50. Therefore, it is concluded that a rigidly defined age criterion for cardiac transplant recipients is not acceptable. Each potential recipient must be evaluated in terms of individual risk and benefit from the procedure.

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Over the past two decades, the results of cardiac transplantation have steadily improved. As the procedure was developed and centers were established to perform the procedure, rigid criteria for the selection of potential recipients were adopted in an effort to achieve the best results possible. Recently, these criteria have been modified to include a group of patients who were otherwise eligible but were over the age of 50 years. To determine the results of cardiac transplantation in this older age group, we reviewed our series of patients for a 6 year period, focusing specifically on those over 50 years of age.

Methods

Patients. From March 1979 to March 1985, 323 patients were referred for possible cardiac transplantation at the University of Arizona (Table 1). The hospital records of all patients accepted for transplantation and those having cardiac transplantation were retrospectively reviewed.

Each candidate was carefully evaluated by complete history and physical examination, review of all referring information, radiologic and hemodynamic data, multisystem laboratory tests and immunologic studies. Psychologic and social evaluations were also performed. The decision to accept or refuse a candidate was made on an individual basis using standard guidelines other than age. All patients were in New York Heart Association functional class IV and had no secondary organ system disease that would otherwise limit survival. Ninety-three patients were accepted after evaluation and 62 transplantations were performed in 61 patients.

From March 1979 through December 1983, 32 patients were treated with conventional immunosuppressive therapy: azathioprine, prednisone and rabbit antithymocyte globulin (1). Eight of these patients were over 50 years of age. After January 1983, cyclosporine became the main immunosuppressive agent. Five patients over 50 and 25 patients under 50 were managed on a protocol of cyclosporine, low-dose prednisone and rabbit antithymocyte globulin. Details of each protocol have been published previously (2).

Surgical procedures. The operative technique has been previously reported in detail (3). Rejection episodes were

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Table 1. Patients Referred for Cardiac Transplantation, March 1979 to March 1985

Patients	Age (yr) of Patients < 50	> 50	Total
Accepted for transplantation			
Underwent transplantation	49	13	62
Refused transplantation	4	1	5
Awaiting transplantation	4	4	8
Died while awaiting donor	15	3	18
Subtotal	72	21	93
Rejected for transplantation			
Advanced age	0	40	40
Diabetes	5	3	8
Medical contraindication	12	14	26
Other medical therapy offered	9	1	10
Other surgical therapy offered	5	0	5
Others	21	2	23
Subtotal	52	60	112
Miscellaneous patients			
Referred to other centers for transplantation or evaluation	18	5	23
Died before complete evaluation	28	11	39
Undecided, before evaluation	9	5	14
Never presented, no follow-up	27	15	42
Subtotal	82	36	118
Total	206	117	323

diagnosed by routine endomyocardial biopsy and treated with pulse methylprednisolone therapy or rabbit antithymocyte globulin, or both (4,5). Infections were diagnosed and treated as rapidly as possible. Pulmonary lesions were identified by transtracheal aspirate or transthoracic needle aspiration if necessary (6).

Statistics. The Student *t* test was used to determine the differences between groups. The chi-square test was used to assess the significance of differences in event frequency between groups. Significance was determined at a probability less than 0.05. The survival is expressed in actuarial terms. Values are expressed in linearized incidence.

Results

Two hundred six patients under 50 years of age were referred for transplantation to the University of Arizona. Of these, 72 (35%) were accepted and 49 (24%) underwent transplantation. One hundred seventeen patients over age 50 were referred: 21 (18%) were accepted and 13 (11%) underwent transplantation (Table 1).

Eleven men and two women were over 50 years old at the time of transplantation. Their mean age was 53 ± 1 years (range 50 to 57). Forty-two men and seven women were less than 50 years old (mean 36 ± 1, range 13–49).

Clinical features. Ischemic, idiopathic and viral cardiomyopathy form the main groups of cardiac disease in these 62 patients (Table 2). Ischemic heart disease was the principal cause of end stage cardiac disease (9 [69%] of 13 patients) in the group over 50 years. This differs significantly from the younger group of patients in whom ischemic heart disease accounted for less than a third (15 [31%] of 49) of primary cardiac diseases ($p < 0.05$). Patients over 50 years old requiring cardiac transplantation after ischemic heart disease had a mean age of 53 ± 0.5 years, which differs significantly from that in the younger group having ischemic cardiomyopathy (44 ± 1 years, $p < 0.05$). The actuarial survival curves of these patients presenting with ischemic disease were identical in both groups (Fig. 1).

Table 2. Primary Cardiac Disease in 62 Patients Undergoing Transplantation

Cause	Age (yr) of Patients < 50	> 50
Ischemic	15 (31%)*	9 (69%)*
Idiopathic	17 (35%)	3 (23%)
Viral	8 (16%)	1 (8%)
Valvular	2 (4%)	
Postpartum	2 (4%)	
Alcohol	2 (4%)	
Congenital	2 (4%)	
Chronic rejection	1 (2%)	
Total	49	13

*$p < 0.05$.

All patients were in functional class IV and receiving maximal medical management before transplantation. Twelve patients (12 [24%] of 49) under 50 years of age required in-hospital care while awaiting transplantation and seven were receiving inotropic therapy. None of the patients in the older group were hospitalized in the immediate transplantation period.

Figure 1. Actuarial survival of 24 transplant patients (9 patients > 50 and 15 patients < 50 years old) with ischemic heart disease as the primary cause of cardiomyopathy. One year survival was 65 ± 17% for those patients over 50 years and 64 ± 13% for those under 50 years.

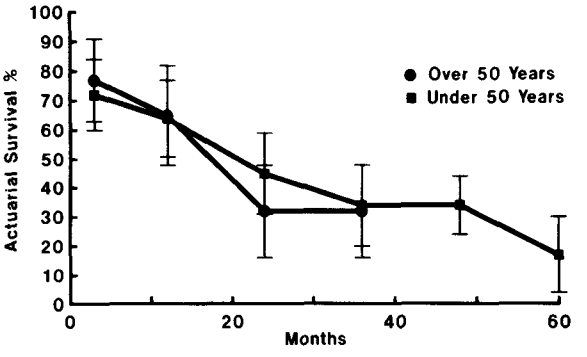

Table 3. Mortality of 62 Patients Undergoing Transplantation

	Age (yr) of Patients	
	< 50 (n = 49)	> 50 (n = 13)
Early mortality		
Preoperative	1 (2%)	1 (8%)
0 to 3 months	8 (16%)	1 (8%)
Total	9 (18%)	2 (16%)
Late mortality		
Greater than 3 months	13 (33%) of 40	4 (36%) of 11

Mortality. The early mortality (0 to 90 days) was 18% for the group under 50 years of age and 16% for the older patients. The late mortality (> 90 days) was 33 and 36%, respectively (Table 3).

The causes of early and late death are summarized in Table 4. In both groups, rejection and infection were the principal causes of death. There was no difference in the incidence of these problems between the two groups.

Infection. The incidence of infection was 1.9 ± 0.4 episodes per patient or 1.4 episodes per patient-year in the group under 50 and 1.9 ± 0.5 episodes per patient or 1.1 episodes per patient-year for those over 50.

Rejection. The incidence of rejection in patients under 50 years was 2.0 ± 0.2 episodes per patient or 1.7 episodes per patient-year. In patients over 50 years old it was 2.2 ± 0.5 episodes per patient or 1.3 episodes per patient-year.

Survival. The mean survival was 17 ± 2 months for patients under and 20 ± 4 months for patients over 50 years of age. The actuarial survival at 1 year was 66 ± 7% for the group under 50 and 72 ± 14% for the group over 50 (Fig. 2).

Table 4. Causes of Death in 62 Patients

	Age (yr) of Patients	
	< 50 (n = 49)	> 50 (n = 13)
Early death (0 to 90 days)		
Acute rejection	4 (8%)	
Infection	2 (4%)	1 (8%)
Donor organ failure	1 (2%)	1 (8%)
Multisystem failure	1 (2%)	
Arrhythmia	1 (2%)	
Total	9 (18%)	2 (16%)
Late death (> 90 days)		
Infection	5 (13%)	
Chronic rejection	3 (7.5%)	1 (9%)
Acute rejection	2 (5%)	2 (18%)
Arrhythmia	1 (2.5%)	1 (9%)
Lymphoma	1 (2.5%)	
Suicide	1 (2.5%)	
Total	13 (33%) of 40	4 (36%) of 11

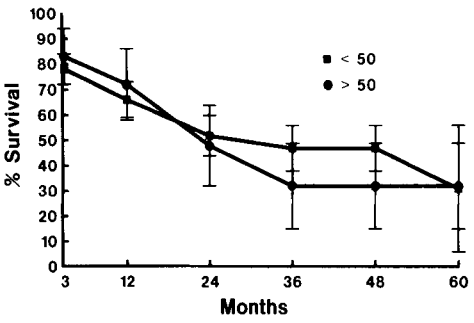

Figure 2. Actuarial survival of 62 transplant patients. One year survival was 66 ± 7% for those patients under 50 and 72 ± 14% for those over 50 years old.

Discussion

Because of the high mortality rate associated with cardiac transplantation in the early days of the procedure, strict criteria for recipient selection were established to achieve the best results possible. Those criteria, combined with the continued gain in knowledge and accumulated clinical experience, have permitted the establishment of cardiac transplantation as a valuable therapeutic method, improving both the quantity and quality of life (1,2,7–13).

Age as a predictor of survival. Still, the age of the recipient is considered to be a significant predictor of survival. The 1984 Report of the International Heart Transplantation Registry (14) provided data on 1,076 patients from 44 centers (1968 to 1984) and reported 6 year actuarial survival rates (excluding 30 day mortality) of 28% for patients more than 50 years of age, 34% for patients between 40 and 49 years of age and 51% for patients aged 30 to 39 years. Patient age, the expertise of the center and the use of cyclosporine were the most significant predictors of survival (14). It is notable that in our experience the type of immunosuppressive regimen employed does not affect survival (2).

Criteria for selection. In 1982, Pennock et al. (15) reported that only 11% of 1,225 patients referred for evaluation were ultimately accepted for transplantation. Patients older than 50 years were found to have a 1 year survival rate of less than 40%. In our program, 29% of all patients referred for evaluation have been accepted and 19% have undergone transplantation. Forty referred patients have been rejected mainly on the basis of advanced physiologic age characterized by advanced chronologic age and evidence of decreased function of secondary organ systems unrelated to cardiac function. Of the referred patients over 50 years old, 18% have been accepted and 11% have undergone transplantation. In our selection process, age is not a contraindication, yet it remains an important selection factor as demonstrated by the lower percentage of patients accepted and finally undergoing transplantation in this group (16).

Mortality and survival: role of age. It is interesting that the mortality and complications, as well as survival, do not differ from one age group to the other. The etiology of end stage heart failure (ischemic versus others) did not affect survival in our study. Aside from a greater proportion of patients with ischemic heart disease in the older group, the only significant difference between the two groups was the number of patients under 50 years requiring pretransplantation in-hospital care and inotropic therapy. This would indicate that a more aggressive approach to end stage cardiac disease was taken in younger patients.

Although the primary objective of cardiac transplantation is patient survival, the quality of life for these patients is equally important. We are pleased to observe that the success of rehabilitation is excellent in both groups.

Conclusions. The results of cardiac transplantation are not significantly different for those patients over and under 50 years of age. Thus, a rigidly defined age criterion for potential cardiac recipients is currently unacceptable. A large number of patients over 50 years of age with severe nonsurgical ischemic heart disease may be considered candidates for cardiac transplantation if physiologic age is not advanced by disease of other organ systems which may limit survival. We believe that every potential recipient must be evaluated individually in terms of the risk and benefit from cardiac transplantation.

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